Genetic Network Modeling

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A cell processes genetic information through transcription and translation of its genes. Understanding the organization of the genetic network and its minimum complexity requirement is among the important theoretical questions about the origins and evolution of life. With the advent of large-scale gene recognition techniques such as GeneChip and MicroArray, theoretical modeling of the genetic networks will also have applications in the biotechnology industry.

In the first project, Boolean networks are used to address complex problems in the cell cycle. First, a general strategy is formulated to generate Boolean genetic networks that incorporate all relevant biochemical and physiological parameters and cover all of their regulatory interactions in a deterministic manner. Second, "realistic Boolean genetic networks" are introduced that produce time-series measurements very similar to those detected in actual biological systems. This project will lead to a better understanding of constraints required for modeling a realistic gene network.

A related project addresses the question of whether it is possible, in principle, to completely infer a complex regulatory network architecture from input-output patterns of its variables. This possibility is investigated again using the Boolean networks. Trajectories, or state transition tables of Boolean nets resemble time-series of gene expression. By systematically analyzing the mutual information between input states and output states, the sets of input elements controlling each element or gene in the network are inferred. This process is unequivocal and exact for complete state transition tables. The Reverse Engineering Algorithm based on information theory is implemented in a C program for a 50-element network with three inputs per element. The simulations show that a network can be completely reconstructed using only a surprisingly small amount of expression data. The method developed in this work will lead to a practical way of constructing computer models of gene networks. Although this study is limited to synchronous Boolean networks, the algorithm is generalizable to include multistate models, essentially allowing direct application to realistic biological data sets. The ability to adequately solve the inverse problem may enable in-depth analysis of complex dynamic systems in biology and other fields.

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